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STATEMENT IN SUPPORT OF THE OPPOSITION OF IPS AGAINST EP PATENT 0 939 121 (EP Application 99100703.0) IN THE NAME OF F. HOFFMANN-LA ROCHE AG

An opposition is filed against the above-referred patent on the grounds of:

- Article 100(a) EPC,
- Article 100(b) EPC
- Article 100(c) EPC,

and more particularly on the grounds :

- that the subject-matter of European Patent EP 0 939 121 is not patentable within the term of Articles 52, 54, and 56 EPC,
- that the European Patent EP 0 939 121 does not disclose invention in a manner sufficiently clear and complete in order to be carried out by a person skilled in the art (Article 83 EPC)
- that the subject-matter of the European Patent EP 0 939 121 extends beyond the content of the application as filed (Article 76(1) EPC).

The opposition is based on following documents:

D1 : EP 0 398 327
D2 : EP 0 314 317
D3 : Smith et al., (1990) Science 248, 1019-1023
D4 : Heller et al., (1990) *Biochemistry*, **87**, pp 6151-6155
D5 : EP 0 325 224
D6 : Lesslauer declaration in USSN° 08/095,640,
D7 : Evans *et al.*, (1994) *J. Exp. Med.* **180**, pp 2173-2179
D8 : Third auxiliary request in appeal proceedings against EP 0 471 701
D9 : Fisher *et al.*,(1996) *N. Engl. J. of Med.* **334**, pp 1697-1702
D10 : EP 0 464 533
D11 : Notification of the Examiner dated 24.10.2000 during the prosecution
D12 : CH 331 989 (Priority)
D13 : CH 74 690 (Priority)
D14 : CH 134 790 (Priority)
D15 : Dembic et al., (1990) Cytokine, 4, p231-237
D16 : EP 0 418 014
D17 : EP 0 315 062
D18 : Hsu et al., (1993), *J. Biol. Chem.* 268, 16430-16436

References made hereinafter to the patent application as filed refer to EP 0 939 121 A2.

It is therefore requested that the patent be revoked in full for lack of novelty (Article 54 EPC), lack of inventive step (Article 56 EPC), lack of industrial application (Article 52(4) EPC), insufficiency of disclosure (Article 83 EPC) and for extension beyond the content of the application as filed (Article 76(1) EPC).

It is requested that oral proceedings be scheduled in case the Opposition Division would intend not to follow the request of the Opponent.

I - THE PATENT

The opposed patent relates to TNF-binding proteins (TNF-BPs). We provide a brief summary of the work that is disclosed in the patent application as filed and the examples therein because a comparison of this and the broadly defined subject matter of the claims is relevant for the consideration of sufficiency and also inventive step.

The patentee isolated fractions, which showed TNF binding activity, from HL60 cell extracts. These fractions were further purified by HPLC and then subjected to SDS-PAGE. As a result of the SDS-PAGE, 5 bands (34 kD, 36 kD, 38 kD, 51 kD and 55 kD) were shown to have TNF binding activity (Example 6). In another experiment, 2 additional bands (65 kD and 75 kD) with TNF binding activity appeared in the SDS-PAGE. The bands from the SDS-PAGE were isolated and N-terminally sequenced. Fragments that were obtained by protein digestion of the isolated proteins were also sequenced.

Sequence fragments were determined for the 55 kD, the 51 kD, the 38 kD, the 65 kD and the 75 kD proteins. The sequencing of the 65 kD protein revealed an N-terminal sequence of 18 amino acids in length in which one of the amino acids could not be determined.

Further 7 sequences of the "75(65) kD-TNF-BP" of between 4 and 18 amino acids in length are disclosed in the application. In 2 of the sequences one amino acid could not be determined (Example 7).

With the help of the N-terminal sequences the full-length cDNA sequence for the 55 kD TNF-BP was determined (Fig. 1). For the 75 / 65 kD TNF-BP only a partial sequence was identified (Fig. 4 – see also Example 8). This partial sequence codes for a truncated 75 / 65 kD TNF-BP which lacks the first 48 amino acids from the mature TNF-BP plus another 22 amino acids which code for the signal peptide.

Only the 55 kD TNF-BP was then expressed in COS cells (Example 9) and in insect cells (Examples 10 and 11).

In summary the 75 / 65 kD TNF-BP full length cDNA was neither isolated nor was the protein or fragments thereof expressed let alone fusion proteins of the 75 / 65 kD TNF-BP. There is no technical teaching whatsoever on the construction, the advantage or the use of TNF-BP-Ig fusion proteins. The only hint in the application as filed to fusion proteins is a "boiler plate"-like general statement on p7, lines 18 – 24.

> *"Die Erfinding betrifft weiterhin DNA-Sequenzen, die eine Kombination aus zwei Teil-DNA-Sequenzen umfassen, wobei die eine Teilsequenz für solche löslichen Fragmente von nicht-löslichen Proteinen, die TNF binden kodiert (s.o.) und die andere Teil-Sequenz, für alle Domänen ausser der ersten Domäne der konstanten Region der schweren Kette von humanen Immunoglobulinen, wie IgG, IgA, IgM bzw. IgE, kodiert."*

II - THE CLAIMED SUBJECT-MATTER OF EP 0 939 121

EP 0 939 121 claims DNA sequences comprising a combination of two partial DNA sequences:

- one of these coding for soluble TNF-binding fragment of an insoluble protein being selected from DNA sequences coding for:
  - soluble fragments of a TNF-BP protein having an apparent molecular weight of 75 / 65 kD
  - the protein of 75 / 65 kD being one encoded by a DNA sequence containing the partial cDNA shown in figure 4
  - the protein including the N-terminal sequence IID
- the other partial sequence coding for all domains except the first domain of the constant region of the heavy chain of human immunoglobulins of class IgG.

It should be noted that the wording of claim 1 is open, meaning that DNA sequences may contain other sequences or fragment of sequences.

Dependent claim 2 refers to the Ig_1 and Ig_3 sub-classes of IgG immunoglobulins.

Claims 3 to 6 are directed to recombinant proteins encoded by this DNA, vectors containing these proteins and hosts systems containing the vectors.

The process of claim 7, covers a process for the production of such a protein according to claim 3 by cultivating a transformed host system and isolating said compound from either the host system or the medium.

Claim 8 is a product-by-process claim, i.e. directed to the compound obtainable by the process of claim 7.

Claim 9 is directed to pharmaceutical preparations which are also open worded as they contain one or more proteins according to claim 3 or 8.

Claims 10 to 12 are directed to the use of such a protein according to claim 3 or 8 for the production of a pharmaceutical preparation (claim 10), for the identification of TNF in serum or other biological fluids as a diagnostic (claim 11), and for the detection of TNF agonists and TNF antagonists (claim 12).

III - ON THE EXTENSION BEYOND THE APPLICATION AS FILED

- Claim 10

Claim 10 as granted relates to:

The use of a compound in accordance with claim 3 or 8 for the production of a pharmaceutical preparation for the treatment of pathological conditions in which TNF is involved as a mediator of immune response or inflammation.

The application as filed, however, only discloses that TNF-BPs of the invention may be used for the preparation of pharmaceutical preparations for the treatment of illnesses in which TNF is involved (p6 lines 52-58) It is neither disclosed in the application as filed that TNF-BPs can be used for the production of a pharmaceutical preparation for the treatment of pathological conditions in which TNF *is involved as a mediator of immune response or inflammation* nor are there specific illnesses which can be treated with the TNF-BPs claimed listed anywhere in the application as filed. The statement referring to the prior art on page 2 regarding assumptions concerning the involvement of TNF together with other cytokines in a series of pathological conditions cannot take the place of a disclosure concerning treatments using the fusion protein of a part of TNF-BP and a part of

immunoglobulin against TNF as mediator of immune response or inflammation on which a claim can be based.

Claim 10 extends beyond the content of the application as originally filed. It infringes therefore Article 76(1) EPC.

IV – ON THE INSUFFICIENCY OF DISCLOSURE

- About claim 1

Claim 1 of the subject patent covers DNA sequences which comprise a fusion between two sequences, the first one being derived from the 75 / 65 kD TNF-BP and the second one coding for specific domains of immunoglobulins.

The full length 75 / 65 kD TNF-BP is not disclosed in the application. The truncated sequence that is provided in Fig. 4 lacks the 48 N-terminal amino acids of the mature protein and in addition the 22 amino acids of the signal peptide. The TNF-BPs fold into several cysteine-rich domains (CDRs), and all CDRs are required for TNF binding to the receptors (D18). Thus, the application does not teach the skilled person how to produce a functional TNF-BP fusion protein.

The preparation and assembly of such sequences to obtain a functional fusion protein is not even disclosed in a general way in the patent.

- About claim 2

Claim 2 of the subject patent covers the specific species of DNA sequences, namely those wherein Ig1 or Ig3 human immunoglobulins are encoded by the 2nd part of the DNA. However nothing is disclosed in the patent concerning a specific use of these sub-types of immunoglobulins to construct the combination of DNA sequences according to the invention.

Therefore, this patent does not disclose this invention in a manner sufficiently complete for it to be carried out by a person skilled in the art.

- About claims 9 and 10

Claim 9 is directed to pharmaceutical preparations, especially for the treatment of illnesses where TNF is involved. Claim 10 is directed to such preparations for the treatment of pathological conditions where TNF is involved as a mediator of immune response or inflammation.

While the proprietor of the patent made reference to the excellent effect of a fusion protein covered by the claims, named ENBREL during prosecution, he conveniently failed to

inform the Examining Division that the same protein, compared to the p55 TNFR/IgG fusion protein, shows only 10% survival in a murine model of gram negative sepsis. These data come from a declaration submitted in the US application relating to the p55 TNFR/IgG fusion protein (D6) and are backed up by D7. In addition, the clinical trials with ENBREL in sepsis have failed, another fact proprietor forgot to mention, when praising ENBREL as so successful in the treatment of rheumatoid arthritis (D9).

In view of the above, the invention is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, as claims 9 and 10 include embodiments which would not only be inoperable, but outright dangerous to the health of a patient, e.g. one suffering from sepsis who is treated with such a pharmaceutical preparation.

- About claim 11

Claim 11 is directed to the use of fusion protein according to claim 3 or 8 for the production of a pharmaceutical preparation for the treatment of pathological TNF-associated conditions.
There is no disclosure in the opposed patent teaching a man skilled in the art how to use a compound of claim 3 or 8 as a diagnostic for the identification of TNF in serum or other body fluids, beyond a remark that this is to be done with methods known in the art.
Thus, claim 11 is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

- About claim 12

Claim 12 is directed the use of fusion proteins for the detection of TNF antagonists or agonists. No indication is given concerning the way for the man skilled in the art to find such agonists or antagonists, despite the fact that the use of soluble Ig fusion proteins for the detection of TNF agonists or antagonists was not known in the art. The source of a potential agonist or antagonist let alone an assay suitable for the detection of an agonist or antagonist is not described.
In view of the above, the invention as claimed in claim 12, is not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

V – ON THE ENTITLEMENT OF PRIORITY

The subject matter of all granted claims is not entitled to priority.

Indeed none of the three priority documents D12, D13, D14 discloses DNA sequences combining sequences from a part of TNF-BP and a part of another domain more particularily of an immunoglobulin. This fact is not even suggested in these applications. This conclusion has also been established during the examination proceedings (Notification of the examiner of 24.10.2000, D11).

As the feature appears to be an essentially feature of the compound, the claims as granted cannot benefit from the priority of CH 331989 (D12), CH74690 (D13), CH 134790 (D14).

The date which should be taken into consideration for the evaluation of the prior art according to Articles 54 and 56 EPC is the filing date of the European application, i.e. August 31, 1990.

VI - ON THE LACK OF NOVELTY

A. Over D16 : EP 0 418 014 under article 54(3) EPC

D16, having a priority of September 11, 1989, discloses a TNF-R and, among others, biologically active molecules, i.e. particular molecules being capable of binding detectable quantities of TNF for example as a component of a hybrid receptor construct. (page 4, lines 48-51). The sequence of the TNF-R of D16 is identical to the sequence disclosed and claimed for the soluble TNF binding protein in the opposed patent.
D16 specifically discloses that a recombinant chimeric antibody molecule may also be produced having TNF-R sequences substituted for the variable domains of either both of the immunoglobulin molecule heavy and light chains and having unmodified constant region domains. D16 discloses in particular, an example of a chimeric TNF-R/IgG1 that may be constructed according to the invention (page 8, lines 18-25). D16 refers to EP 0 315 062 where additional details concerning the way of producing these chimera are disclosed. In line with the Guidelines C-IV 6.1(ii) EP 0 315 062 is also content of D16. EP 0 315 062 in particular, this document discloses that the replacement gene may encode all or a portion of an immunoglobulin constant region having a particular effector function, class and/or origin, including IgG constant regions (page 6, lines 32-35). This is obviously understood by the skilled person to read on Fc portions of an immunoglobulin since they have a particular effector function. EP 0 315 062 is annexed to the present statement under the reference D17. Thus, D16 discloses fusion proteins comprising the 75 / 65 kD TNF-BP and an IgG Fc portion. The Fc portion is defined in the art as all domains but the first domain of

the constant region of an immunoglobulin.
In view of the above, claim 1 of the opposed patent is anticipated by D16.

Claim 2 is dependent on claim 1, which lacks novelty. The additional feature recited by this claim is the definition of the IgG_1 or IgG_3 subtype of. However, fusion proteins of the IgG_1 subtype are also disclosed in D16 on page 8, line 20.
In view of the above, claim 2 is anticipated by D16.

Claim 3 is dependent on claims 1 and 2, which lack novelty. Claim 3 is directed to a protein encoded by the DNA sequences disclosed in claim 1.
D16 discloses chimeric proteins obtained by transcription and translation of the chimeric TNF-R/Ig molecule.
In view of the above, claim 3 is anticipated by D16.

Claim 4 is dependent on claims 1 and 2 which lack novelty. Vectors expressing the desired protein, which are suitable for prokaryotic or eukaryotic hosts, are also disclosed in D16 (page 8, lines 30-50).
In view of the above, claim 4 is anticipated by D16.

Claim 5 is dependent on claim 4, which lacks novelty. Prokaryotic and eukaryotic host systems transformed with a vector containing DNA sequences encoding the desired protein are also disclosed in D16 (page 9, lines 15-18).
In view of the above, claim 5 is anticipated by D16.

Claim 6 is dependent on claim 5, which lacks novelty. Mammalian cells and insect cells as host systems are disclosed in D16 (page 10, lines 23-34).
In view of the above, claim 6 is anticipated by D16.

Claim 7 is dependent on claims 3, 5 and 6 which lack novelty. Cultivating a host system and isolation of the protein is disclosed in D16 (page 11, lines 35-40, lines 51-56).
In view of the above, claim 7 is anticipated by D16.

Claim 8 is dependent on claim 7, which lacks novelty. Recombinant production of the proteins is disclosed in D16 (page 11, lines 24-27).
In view of the above, claim 8 is anticipated by D16.

Claim 9 is dependent on claims 3 and 8, which lack novelty.

Pharmaceutical compositions comprising as active ingredients an effective amount of TBP-R are disclosed in D16 (page 12, lines 15-18).
In view of the above, claim 9 is anticipated by D16.

Claim 10 is dependent on claims 3 and 8, which lack novelty. D16 discloses the use of the proteins to suppress TNF-dependent inflammatory responses in humans (page 12, lines 15-18)
In view of the above, claim 10 is anticipated by D16.

B. *Over D1 : EP 0 398 327 under article 54(3) EPC*

D1, having a priority of May 18, 1989, discloses a TNF-BP and, among others, functional derivatives thereof (page 6, lines 22-27). The sequence of the TNF-BP of D1 is identical to the sequence disclosed and claimed for the soluble TNF binding protein in the opposed patent.
D1 specifically discloses that the functional derivatives cover derivatives, which may be prepared, among others, from the N- or C-terminal groups, by means known in the art, and are included in the invention as long as they remain pharmaceutically acceptable and do not confer toxic properties on compositions containing it.
Moreover D1 discloses in its specification that the present invention encompasses a protein comprising the TNF-BP (called TBP-II) sequence as well as any other polypeptide of TBP-II in which one or more amino acids are added thereto (page 4, lines 3-6).

Claim 1 of the opposed patent is unclear in that it does not define the domains that may be added to the fragment of TNF-BP.
As a matter of fact, 4 different interpretations may be given to claim 1 as the domain to be fused to the fragment of TNF-BP may be:

A. a domain of a protein (except for the first domains of the constant region of the heavy chain of a human immunoglobulin of class IgG)
B. a domain of human immunoglobulin of class IgG (except for the first domains of the constant region of the heavy chain of this immunoglobulin)
C. a domain of the heavy chain of an human immunoglobulin of class IgG (except for the first domains of the constant region of the heavy chain of this immunoglobulin)
D. a domain of the constant region of the heavy chain of an human immunoglobulin of class IgG (except for the first domains)

Case law is constant on the fact that if the meaning of a claim is not clear, the broadest interpretation of this claim has to be used.

It results therefore that the TNF-BP functional derivatives which are fusion proteins of TNF-BP with another domain, destroy the novelty of claim 1.

Claim 1 of the opposed patent relates to DNA sequences with two partial sequences, one encoding a soluble TNF binding fragment of an insoluble protein (p75 TNFR) including a specified N- terminal sequence, and the other sequence encoding a sequence of a human immunoglobulin. D1 also discloses recombinant production of the TNF binding protein, as well as pharmaceutical compositions containing it.

Claim 2 is dependent on claim 1, which lacks novelty. The additional feature recited by this claim is the definition of the subclass of Ig. However, this definition is also included in the functional derivatives prepared from the C-terminal groups according to claim D1
In view of the above, claim 2 is anticipated by D1.

Claim 3 is dependent on claims 1 and 2, which lack novelty. Claim 3 is directed to a protein coded by sequences disclosed in claim 1.
D1 discloses functional derivatives of the protein TNF-BP.
In view of the above claim 3 is anticipated by D1.

Claim 4 is dependent on claims 1 and 2 which lack novelty. Vectors expressing the desired protein, which are suitable for prokaryotic or eukaryotic hosts, are also disclosed in D1.
In view of the above, claim 4 is anticipated by D1.

Claim 5 is dependent on claim 4, which lacks novelty. Prokaryotic and eukaryotic host systems transformed with a vector containing DNA sequences encoding the desired protein are also disclosed in D1 (page 3, lines 8-13, page 5, lines 23-26).
In view of the above, claim 5 is anticipated by D1.

Claim 6 is dependent on claim 5, which lacks novelty. Mammalian cells as the host systems are disclosed in D1 (page 5, lines 55-58). In view of the above, claim 6 is anticipated by D1, at least for the mammalian cell host systems.

Claim 7 is dependent on claims 3, 5 and 6 which lack novelty. Cultivating a host system and isolation of the protein is disclosed in D1 (page 6, lines 8-12).
In view of the above, claim 7 is anticipated by D1.

Claim 8 is dependent on claim 7, which lacks novelty. Recombinant production of the

proteins is disclosed in D1 (page 6, lines 8-12).
In view of the above, claim 8 is anticipated by D1.

Claim 9 is dependent on claims 3 and 8, which lack novelty.
Pharmaceutical compositions comprising as active ingredients the proteins TBP-II are disclosed in D1 (page 7, lines 20-22).
In view of the above, claim 9 is anticipated by D1.

Claim 10 is dependent on claims 3 and 8, which lack novelty. D1 discloses the use of the proteins for treatment of, among others, septic shock and auto-immune diseases (page 7, lines 23-26)
In view of the above, claim 10 is anticipated by D1.

VII – SUBSIDIARILY: ON THE LACK OF INVENTIVE STEP

A. Of CLAIM 1 :

1. Over D3 :

The soluble 75 / 65 kD TNF-BP was already state of the art, as it was disclosed in D3, which was published prior to the effective date of the opposed patent. The full length 75 / 65 kD TNF-BP was disclosed in D3.

Indeed, during the prosecution, D3 (numbered D11 in the prosecution) was held to be the closest prior art. It can be agreed to this. In light of this closest prior art, the patentee formulated the problem to be solved in its submission during the Examination from October 1, 2002 *"to provide a TNF-BP-derivative for the production a pharmaceutical preparation for the treatment of diseases where TNF is involved"*. The alleged solution of this problem would be the provision of a fusion protein comprising a soluble fragment of the 75 / 65 kD TNF-BP and all domains but the first domain of the constant region of the heavy chain of human IgG. What is the technical effect of the feature "fused to a soluble fragment of the 75 / 65 kD TNF-BP and all domains but the first domain of the constant region of the heavy chain of human IgG" that is distinguishing over the prior art D3? There is no hint in the application as filed as to any technical effect.
The alleged invention appears therefore nothing more than an alternative to D3, resulting from an arbitrary fusion with a IgG domain. Such a solution is clearly lacking of inventive step. Therefore the problem put forward by the patentee during prosecution is apparently not

the real problem to be solved by the in invention. It is a result of a hindsight view in light of the later provided data.

2. Over D4 and D5 :

Moreover, if we start from D4 as the closest prior art, this document discloses a partial DNA sequence of the insoluble protein, i.e. the p75 TNFR, which overlaps to a great extent with the partial DNA sequence shown in Fig. 4 of the opposed patent, which also shows a partial sequence of the p75 TNFR. The soluble forms are also described in D4, including their TNF-binding activity and their identity to the soluble TNF binding proteins of D3.

In view of D4, the technical problem to be solved would be to find an alternative to the existing soluble forms of TNF-BP.D5 deals with the production of soluble mimetic receptors by generating immunoglobulin fusion proteins, and proposes these immunoglobulin-fusion proteins as effective therapeutic proteins.In particular, D5 discloses soluble receptor-Ig fusion proteins for therapeutic use. The parts of the receptors employed in D5 for the fusion proteins belong to the same receptor family as the TNF receptor, in particular the EGF receptor. Thus, e.g. in column 11, lines 51-54, D5 discloses a construct having a sequence encoding a dimerizing protein joined to a sequence encoding a receptor analog. Portions of immunoglobulin sequences are preferred dimerizing proteins (column 12, l. 12-14). Even the heavy chain hinge region and portions thereof are mentioned as being preferred (column 12, l. 9-22).
The Ig fusion construct described in D5 is identical to the one in the opposed patent, the only difference being that the soluble receptor part is not TNF-R but a protein from the same family as the TNF receptor.
Knowing the prior art of D4, a skilled person, faced with the technical problem of providing alternative TNF-BP would take account the teaching of D5 and by combining it with D4, would construct an Ig fusion with TNF-BP.

In particular, D4 and D5 are in the same field as the alleged invention, i.e. soluble receptor proteins; and a combination of their teachings solves the problem, namely namely alternative TNF-BPs.
In view of the above, Claim 1 does not involve an inventive step over D4, in combination with D5.

3. Over D4 and D10 :

The obviousness results also from document D10, which relates to fusion proteins of cytokine receptors, i.e the family comprising the TNF receptors with constant domains of

the immunoglobulin and more preferably of the constant part of the heavy chain of human IgG1.
In view of the above, Claim 1 does not involve an inventive step over D4, in combination with D10.

B. Of CLAIMS 2 to 8 :

Claims 2-8 are all dependent directly or indirectly on claim 1, which does not involve an inventive step, and relate to recombinant production of the proteins and the proteins per se.
Seeing that the soluble TNF-binding fragments are known from D3, and the recombinant production of fusion proteins is described either in D5 or in D10, while the recombinant production of the soluble TNF-binding fragments is described in D4, no inventive step is involved in claims 2-8 over D4, in combination with D3 and D5.

C. OF CLAIMS 9 AND 10 :

Claims 9 and 10 depend on claims 3 and 8, which do not involve an inventive step. The use of the soluble TNF-binding fragments as inhibitory molecules for TNF is disclosed in D3. The recombinant production of these fragments is described in D4 and the recombinant production of the fusion proteins is described in D5. Thus no inventive step is involved in claims 9 and 10 over the combination of D3, D4 and D5.

D. OF CLAIMS 11 AND 12 :

D10 discloses that the use of TBP-II and its functional derivative are indicated for antagonizing the deleterious effects of TNF in mammals (page 7, lines 15-21). The function of TBP-II and protein containing a part of TBP-II are therefore known as potential antagonist of TNF activity.
In view of D10, it would be obvious to try, with a reasonable expectation of success, to determine the presence of TNF or to find antagonists and agonists as well
Thus no inventive step is involved in claims 11 and 12 over D10.

VIII – ON THE LACK OF INDUSTRIAL APPLICATION

Claim 11 covers the use of the fusion protein as a diagnostic for identification of TNF in serum or other body fluids. This claim reads on the diagnostic use performed on the human body, i.e. refers to a diagnostic method on the human body.
However, diagnostic methods practised on the human body are not regarded as inventions susceptible of industrial application.

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Claim 11 covering a diagnostic method is therefore not patentable under article 52(4) EPC.

It is requested therefore that the patent be revoked in whole on the basis of article 52, 54, 56, 83 and 76(1) EPC.

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